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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FRONDA, CHRISTIAN L	
ART UNIT	PAPER NUMBER
1652	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/598,873	OSSWALD ET AL.	
	Examiner	Art Unit	
	CHRISTIAN L. FRONDA	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *1-9,12-25,27 and 28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,11 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/01/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of Invention 4 and SEQ ID NO: 1 in the reply filed on 09/29/2008 is acknowledged, where claims 10, 11, and 26 read on elected SEQ ID NO: 1. Upon further consideration polynucleotides encoding SEQ ID NOs: 2, 3, and 5 and the polynucleotide of SEQ ID NO: 4 will be examined with elected SEQ ID NO: 1, where these polynucleotides are transformed into the recited host cell.

Claims 1-9 and 12-25, 27, and 28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention. The requirement is still deemed proper and is therefore made FINAL.

2. Claims 10, 11, and 26 which read on SEQ ID NOs: 1-5 are under consideration in this Office Action.

3. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

4. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

5. Claims 10, 11, and 26 are objected to for depending from non-elected claim 9 and reciting non-elected subject matter. Applicants are required to amend the claims to recite the elected subject matter of SEQ ID NO: 1 and rewrite the claim as an independent claim.

Claim Rejections - 35 U.S.C. § 112, 2nd Paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 10, 11, and 26 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 recites the phrase "within the scope of the degeneracy of the genetic code" which renders the claim vague and indefinite. The metes and bounds of the claim are uncertain since the specific nucleotide sequence of the polynucleotide encompassed by the claim is unclear. Appropriate correction is requested. Claims 11 and 26 are also rejected because they do not correct the defect of claim 10.

Claim Rejections - 35 U.S.C. § 112, First Paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 10, 11, and 26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants are directed toward the USPTO Written Description Training Materials made available to the public on 04/11/2008 for information regarding examination of patent claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph.

The claims are genus claims encompassing a process for the enzymatic preparation of amides from nitriles using a genus of polynucleotides encoding polypeptides having cyanide-tolerant nitrile hydratase activity and amino acid sequences which are 90%-100% identical to SEQ ID NOs: 2, 3, or 5; a genus of polynucleotides comprising functionally neutral sense

mutations of SEQ ID NO: 1 or 4 and encoding a cyanide-tolerant nitrile hydratase; and a genus of polynucleotides the hybridize to the complementary sequences of SEQ ID NO: 1 or 4 under the recited stringent conditions of washing in 5XSSC at a temperature from 50-65°C and encode a cyanide-tolerant nitrile hydratase.

The scope of each genus includes many members with widely differing structural, chemical, and physiochemical properties including widely differing nucleotide and amino acid sequences. Furthermore, each genus is highly variable because a significant number of structural and biological differences between genus members exist.

The recitation of the polynucleotides encoding polypeptide having an amino acid sequence which are 90%-100% identical to SEQ ID NOs: 2, 3, or 5 and having cyanide-tolerant nitrile hydratase activity represents a partial structure. That is, the claimed polypeptides share at least 90% of the structure of SEQ ID NOs: 2, 3, or 5, while 10% of the structure can vary. However, there is no teaching in the specification regarding which 10% of the structure of the polypeptide can be varied while retaining cyanide-tolerant nitrile hydratase activity.

While the specification discloses the polynucleotides of SEQ ID NOs: 1 and 4 and the polypeptides of SEQ ID NOs: 2, 3, and 5; the specification, however, does not describe and define any structural features, nucleotide/amino acid sequences, and/or biological functions that are commonly possessed by members of each genus. The specification does not provide any correlation between any structure and cyanide-tolerant nitrile hydratase activity, other than SEQ ID NOs: 2, 3, and 5, based on which those of ordinary skill in the art could predict which amino acid sequences and structures are responsible for cyanide-tolerant nitrile hydratase activity that can be altered to have an amino acid sequence having 90-100% sequence identity. There is no art-recognized correlation between any structure and cyanide-tolerant nitrile hydratase activity, other than SEQ ID NOs: 2, 3, and 5, based on which those of ordinary skill in the art could predict which amino acid sequences and structures are responsible for cyanide-tolerant nitrile hydratase activity that can be altered to have an amino acid sequence having 90-100% sequence identity.

MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the

variation within the genus. In this case, the specification fails to disclose additional polynucleotides encoding polypeptides having cyanide-tolerant nitrile hydratase activity as encompassed by the claims.

Vas-Cath, Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class, where the specification provided only the bovine sequence.

In view of the above considerations, one of skill in the art would not recognize that applicants were in possession of the each claimed genus.

10. Claims 10, 11, and 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process for the enzymatic preparation of amides from nitriles using a host cell transformed with the polynucleotide of SEQ ID NO: 1 or 4 or polynucleotide encoding the a cyanide-tolerant nitrile hydratase having the amino acid sequence of SEQ ID NOs: 2, 3, or 5; does not reasonably provide enablement for any other embodiment as recited in the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

According to MPEP 2164.01(a), factors considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The

quantity of experimentation needed to make or use the invention based on the content of the disclosure.

MPEP§ 2164.04 states that while the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection. The language should focus on those factors, reasons, and evidence that lead the examiner to conclude that the specification fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims. Accordingly, the factors most relevant to the instant rejection are addressed in detail below.

The nature and breadth of the claims encompass a process for the enzymatic preparation of amides from nitriles using any polynucleotides encoding polypeptides having cyanide-tolerant nitrile hydratase activity and amino acid sequences which are 90%-100% identical to SEQ ID NOs: 2, 3, or 5; any polynucleotides comprising functionally neutral sense mutations of SEQ ID NO: 1 or 4 and encoding a cyanide-tolerant nitrile hydratase; and any polynucleotides the hybridize to the complementary sequences of SEQ ID NO: 1 or 4 under the recited stringent conditions of washing in 5XSSC at a temperature from 50-65^{o}C and encode a cyanide-tolerant nitrile hydratase.

The reference of Chica et al. (Curr Opin Biotechnol. 2005 Aug;16(4):378-84; PTO 892) teaches that the complexity of the structure/function relationship in enzymes has proven to be the factor limiting the general application of rational enzyme modification and design, where rational enzyme modification and design requires in-depth understanding of structure/function relationships. The reference of Sen et al. (Appl Biochem Biotechnol. 2007 Dec;143(3):212-23; PTO 892) teaches *in vitro* recombination techniques such as DNA shuffling, staggered extension process (StEP), random chimeragenesis on transient templates (RACHITT), iterative truncation for the creation of hybrid enzymes (ITCHY), recombined extension on truncated templates (RETT), and so on have been developed to mimic and accelerate nature's recombination strategy However, such rational design and directed evolution techniques only enable methods for searching and screening for the recited polypeptides having cyanide-tolerant nitrile hydratase activity and their encoding polynucleotides.

The specification teaches the polynucleotides of SEQ ID NOs: 1 and 4 and the polypeptides of SEQ ID NOs: 2, 3, and 5. However, the specification does not provide guidance, prediction, and working examples for making the polynucleotides encoding polypeptides having cyanide-tolerant nitrile hydratase activity as claimed. The recitation of the polynucleotides encoding polypeptide having an amino acid sequence which are 90%-100% identical to SEQ ID NOs: 2, 3, or 5 and having cyanide-tolerant nitrile hydratase activity represents a partial structure. That is, the claimed polypeptides share at least 90% of the structure of SEQ ID NOs: 2, 3, or 5, while 10% of the structure can vary. However, there is no teaching in the specification regarding which 10% of the structure of the polypeptide can be varied while retaining cyanide-tolerant nitrile hydratase activity. The specification does not provide any correlation between any structure and cyanide-tolerant nitrile hydratase activity, other than SEQ ID NOs: 2, 3, and 5, based on which those of ordinary skill in the art could predict which amino acid sequences and structures are responsible for cyanide-tolerant nitrile hydratase activity that can be altered to have an amino acid sequence having 90-100% sequence identity. There is no art-recognized correlation between any structure and cyanide-tolerant nitrile hydratase activity, other than SEQ ID NOs: 2, 3, and 5, based on which those of ordinary skill in the art could predict which amino acid sequences and structures are responsible for cyanide-tolerant nitrile hydratase activity that can be altered to have an amino acid sequence having 90-100% sequence identity.

Thus, an undue amount of trial and error experimentation must be preformed where such experimentation involves searching and screening a vast number of biological sources for the claimed polynucleotides or making a vast number of mutations to the polynucleotides and determining whether host cells expressing these polynucleotides encode functional cyanide-tolerant nitrile hydratase that can be used in the production of amides from nitriles. General teaching regarding screening and searching for the claimed invention is not guidance for making the claimed invention.

Therefore, in view of the overly broad scope of the claims, the specification's lack of specific guidance and prediction, the specification's lack of additional working examples, the amount of experimentation required, and the teachings of Cowley et al. stated above; it would require undue experimentation for a skilled artisan to make and use the claimed invention. Without sufficient guidance, the experimentation left to those skilled in the art is unnecessarily

and improperly extensive and undue. See *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988).

Conclusion

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Thursday and alternate Fridays between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed can be reached on (571)272-0934. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

13. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Christian L. Fronda/
Primary Examiner
Art Unit 1652